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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/713,889

11/14/2003

Benjamin Levinson

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27162

7590

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EXAMINER

KRISHNAN, GANAPATHY

ART UNIT

PAPER NUMBER

1623

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/713,889	<b>Applicant(s)</b> LEVINSON ET AL.	
	<b>Examiner</b> Ganapathy Krishnan	<b>Art Unit</b> 1623	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 March 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2-5, 8-10 and 34-48 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-5, 8-10 and 34-48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 3/30/2009 has been entered.

The Request for Continued Examination filed 3/30/2009 has been carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1, 6-7 and 11-33 have been canceled.
2. New Claims 38-48 have been added.
3. Remarks drawn to rejections under 35 USC 103(a) maintained in the previous action.

Claims 2-5, 8-10 and 34-48 are pending in the case.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-5, 8-10 and 34-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson (US Patent Pub. No. 2003/0100752) in view of Drummond

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(Annals of New York Academy of Sciences, 1987, 514, 87-95) and Bettelheim et al (General, Organic and Biochemistry, 1998, page 596), all of record.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Robinson teaches tin porphyrin complexed with amino acid (page 45, claim 1), wherein the substitutions R1-R12 can be H, alkyl or alkenyl and could also be substituents that carry amino acid residues (page 46, left column, middle; page 34, left column, paragraph 200). One of the preferred metal ions complexed to the core is Tin (Symbol for Tin is Sn; page 32, paragraph 183). Formulations comprising the porphyrins of Robinson's invention can be optimized to contain between 0.1 and 50 mg (page 33, paragraph 193). The compounds of Robinson can be applied as aqueous solutions (page

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35, paragraph 211). This means that the tin porphyrins of Robinson's invention are water-soluble. Robinson's compounds can have  $\text{CO}_2\text{R}_{13}$ , wherein  $\text{R}_{13}$  can be H, i.e., a COOH group (page 45, right column, line 10) as a substituent for  $\text{R}_8$  and  $\text{R}_{10}$  in his compound of formula I. Mesoporphyrins have a  $-(\text{CH}_2)_2\text{COOH}$  group for  $\text{R}_8$  and  $\text{R}_{10}$ .

The only difference between the instant compounds claimed and that of Robinson is the alkylene group. One of ordinary skill in the art would expect tin mesoporphyrins having the  $-(\text{CH}_2)_2\text{COOH}$  group for  $\text{R}_8$  and  $\text{R}_{10}$  also to be water soluble when complex with amino acids. According to Robinson the water-soluble tin mesoporphyrin analogs complexed with amino acid are useful for treating psoriasis (page 35, paragraph 211).

Drummond, drawn to metalloporphyrins, teaches control of heme metabolism using tin-protoporphyrins (page 87, introduction, last paragraph). Tin protoporphyrin was by far the most potent (page 88, Results and Discussion; page 89). Tin protoporphyrin is structurally similar to tin-mesoporphyrin except that the protoporphyrin has an ethylene side chain. In the mesoporphyrin, the ethylene side chain is saturated (ethylene side chain if saturated becomes ethyl group). According to Robinson (above), the side chain can be an alkenyl or alkyl. When it is alkenyl, the structure is similar to the protoporphyrin as taught by Drummond, which can be converted to ethyl via hydrogenation.

According to Drummond his synthetic heme analogs have novel biological properties and may have useful clinical roles (see Introduction) and tin-protoporphyrins have proved to be innocuous in toxicology studies in animals. Long-term treatment of rats with tin-protoporphyrins resulted in decrease in bilirubin levels (page 90, middle paragraph; page 92, first full paragraph).

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Bettelheim in general teaches that amino acids exist as zwitterions and are polar. This renders them water soluble. From this and the teaching of Robinson, one of ordinary skill in the art will recognize that complexing the tin-porphyrins of Robinson with amino acids will enhance their solubility and also the solubility of the corresponding mesoporphyrins. Robinson also teaches the use of aqueous solutions of the porphyrins for administration.

Based on the teachings of the prior art above, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make tin mesoporphyrins comprising amino acid residues complexed to the porphyrins and their compositions with a reasonable amount of success since structurally close water soluble analogs complexed with amino acids are seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make tin mesoporphyrins as instantly claimed because the structurally analogous water soluble tin porphyrins, as taught by Robinson and Drummond, are not toxic and have useful therapeutic properties and complexing amino acids to the porphyrins would enhance their aqueous solubility and hence their bioavailability.

Even though Drummond teaches protoporphyrins, Robinson's teaching embraces both proto and mesoporphyrins. Proto- and mesoporphyrins are known in the art and are recognized as interchangeable because of their structural similarity. Hence one of ordinary skill in the art would reasonably expect mesoporphyrins as instantly claimed to have the same or substantially similar beneficial therapeutic effects as taught by Robinson and Drummond. One of ordinary skill in the art would also extend the

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teachings of the prior art to making tin mesoporphyrins as instantly claimed in order to look for more active compounds.

***Response to Applicants Arguments***

Applicants have traversed the rejection of record arguing that:

1. The issue presented is whether the art teaches one skilled in the art that the water insoluble mesoporphyrin should be complexed with an amino acid and that such complexing would impart water solubility to tin mesoporphyrin.

2. Robinson does not disclose or suggest such compounds should be complexed with an amino acid and/or that such a complex would be water soluble even though the uncomplexed compound is water soluble.

3. Drummond does not disclose a tin mesoporphyrin and does not disclose or suggest that such a complex would be water soluble even though the uncomplexed compound is water soluble.

4. Bettelheim discloses that some amino acids are water soluble. This does not suggest or render obvious applicants invention.

Applicants' arguments are not found to be persuasive.

Even though Drummond teaches protoporphyrins, Robinson's teaching embraces both proto and mesoporphyrins. Proto- and mesoporphyrins are known in the art and are recognized as interchangeable because of their structural similarity. The compounds of Robinson and Drummond have very closely related structural core. One of the substituents in Robinson's porphyrins is amino acids. Robinson teaches that his compounds can be applied as aqueous solutions (page 35, paragraph 211). This means

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that the tin porphyrins of Robinson's invention including the ones having amino acids as substituents are water-soluble. Since Bettelheim teaches that amino acids are polar and this makes them water soluble it is logical to choose amino acids as substituents from among the substituents taught by Robinson in order to make mesoporphyrins more water soluble. There is suggestion in the prior art as to the preference of amino acids as substitutions and tin as the metal atom in the porphyrin core to make them water soluble. A reasonable expectation of success is also seen based on the teachings of the prior art.

### ***Conclusion***

Claims 2-5, 8-10 and 34-48 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ganapathy Krishnan/  
Examiner, Art Unit 1623

/Shaojia Anna Jiang/  
Supervisory Patent Examiner, Art Unit 1623